

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Variability in survival and post-cardiac arrest care following successful resuscitation from out-of-hospital cardiac arrest



Steve Balian^a, David G. Buckler^a, Audrey L. Blewer^b,
Abhishek Bhardwaj^a, Benjamin S. Abella^{a,*}, the CARES
Surveillance Group

^a Center for Resuscitation Science and Department of Emergency Medicine, University of Pennsylvania, Philadelphia, PA, USA

^b Department of Community and Family Medicine, Duke University School of Medicine, NV, USA

Abstract

Aim of the study: Regionalization of care for out-of-hospital cardiac arrests (OHCA) may improve patient outcomes. We evaluated inter-hospital variations in post-arrest care provision and the relation between hospital case volume and survival in Pennsylvania.

Methods: This retrospective study (2013–2017) used data from adult OHCA cases in Pennsylvania from the Cardiac Arrest Registry to Enhance Survival. Analysis was performed on hospitals reporting greater than 40 cases/5 years with sustained return of spontaneous circulation upon emergency department arrival and survival to hospital admission. We compared post-arrest treatments across hospitals stratified into arrest volume quartiles. Logistic regression models were used to assess the volume-outcome relationship.

Results: We analyzed 3512 OHCA cases admitted to 48 hospitals. Survival to discharge (24–65%) and neurological recovery (15–56%) were highly varied between hospitals. Compared to lower performing hospitals, hospitals with higher survival rates ($\geq 40\%$) performed significantly more coronary angiographies (32% vs. 26%), stenting (17.5% vs. 13%), and ICD placements (12.5% vs. 7.4%). Across volume quartiles, no significant differences were found in percent of treatment provision or outcomes. After adjustment for patient demographics, prehospital and post-arrest care variables, odds of survival and neurological recovery were 43% (OR 1.43; 95% CI, 1.08–1.89) and 51% (OR 1.51; 95% CI, 1.11–2.04) higher in hospitals with greater receiving volumes, respectively.

Conclusions: Hospital case volume is associated with improved patient outcomes. Inter-hospital variability in OHCA outcomes may potentially be addressed by regionalization of care to high volume centers with higher rates of post-arrest care provision and better patient outcomes.

Keywords: Cardiac arrest, Out-of-hospital, Survival rate, Coronary angiography, Hypothermia, Induced, Epidemiology

Introduction

Post-arrest care following resuscitation from out-of-hospital cardiac arrest (OHCA) is a key component of the chain of survival. Despite initial resuscitation following cardiac arrest, cerebral and cardiac dysfunction

may contribute to low rates of survival and neurological recovery, documented as approximately 11% and 9% respectively, in a recent epidemiologic report.¹ Studies have shown a significant association between early hospital-based interventions, such as coronary angiography and targeted temperature management (TTM), with improved survival beyond the hospitalization period.^{2–4} However,

* Corresponding author at: Center for Resuscitation Science, Department of Emergency Medicine, University of Pennsylvania, 3400 Spruce Street, Ground Ravdin, USA.

E-mail address: benjamin.abella@uphs.upenn.edu (B.S. Abella).

<https://doi.org/10.1016/j.resuscitation.2019.02.004>

Received 24 March 2018; Received in revised form 4 January 2019; Accepted 1 February 2019
0300-9572/© 2019 Elsevier B.V. All rights reserved.

aggressive post-arrest care may require respiratory and hemodynamic support, TTM, glucose control, and seizure management in an intensive care setting which may strain hospital resources.^{2,5,6} A multidisciplinary approach with the necessary hospital resources and personnel is therefore required for consistent provision of high-quality care.

The varying survival outcomes in cardiac arrest between regions and hospitals warrants further examination of confounding hospital practices and characteristics.^{7–11} Along with continued low survival rates, the complexity of post-arrest care has prompted calls for regionalization of care to tertiary cardiac centers.^{4,12–17} A study conducted in Copenhagen demonstrated higher relative OHCA mortality in non-tertiary cardiac centers (94% vs 78%, HR = 1.87 [95% CI: 1.62–2.16]) supporting regionalization.¹⁶

Limited U.S. data exist to evaluate variations in hospital-level care and survival for patients following OHCA resuscitation. We hypothesized that inter-hospital variation in post-arrest care and OHCA survival outcomes exists in Pennsylvania (PA). Our objectives included examining key indicators to compare the performance of hospitals in PA, and assessing the association between cardiac arrest volume as a surrogate measure for hospital expertise in post-arrest care, and patient survival and neurological recovery as our outcomes of interest.

Methods

Data source

Our study utilized prospectively collected data from the Cardiac Arrest Registry to Enhance Survival (CARES) in Pennsylvania (PA).¹⁸ Initiated in 2004 by a collaborative effort between the US Centers for Disease and Control and Prevention (CDC) and the Department of Emergency Medicine at the Emory University School of Medicine, CARES has broad U.S. inclusion of OHCA data with a catchment population of more than 100 million people. The repository was designed to improve OHCA survival rates through standardized Utstein style data collection of key performance indicators across the continuum of acute care involving 911 dispatch centers, EMS systems, and receiving hospitals.¹⁹ Additional details about the registry methodology have been published previously.^{20,21} All non-traumatic OHCA events evaluated by EMS were included if resuscitation (cardiopulmonary resuscitation (CPR), defibrillation, vasopressor drugs) was attempted in the pre-hospital setting. The current study was approved by the Institutional Review Board at the University of Pennsylvania through expedited review. Use of CARES data for this project was approved by the Pennsylvania CARES Data Sharing Committee.

Study design and population

This retrospective analysis utilized CARES data, capturing a population of non-traumatic OHCA events that occurred in adult patients ≥ 18 years of age within the study period of January 1, 2013 to December 31, 2017. To be included in the analysis, patients had to achieve sustained return of spontaneous circulation (ROSC) upon emergency department (ED) arrival and survive to hospital admission. This was done to mitigate confounding effects of prehospital care. Receiving hospitals had to admit greater than 40 cases during the 5-year study period. This cut-off was determined based on prior work with a similar methodology, sensitivity analyses performed on different arrest volume cutoffs, and a consensus of the investigators on what constituted a minimum number of annual arrests to minimize influence

of low-volume hospitals.⁸ The primary outcome was survival to hospital discharge. The secondary outcome was survival with good neurological recovery, defined as a Cerebral Performance Category (CPC) of 1 or 2 at time of discharge, a definition employed by prior OHCA investigations.²²

Study variables and definitions

Key variables analyzed included the following patient and hospital data elements: age, gender, race, medical history, arrest witness status, person initiating CPR, arrest etiology, first monitored cardiac rhythm, advanced airway placement, intravenous (IV) access, drug administration, use of mechanical CPR device, response time variables, provision of TTM, coronary angiography, coronary stenting, implantable cardioverter defibrillator (ICD) placement, coronary artery bypass grafting (CABG), transfer status, patient survival to discharge, and neurological outcome at time of discharge. Race was categorized into white, non-white and unknown. Reported percentages were out of the total of all categories. The arrest to ED time interval was visualized graphically for meaningful breaks in the distribution and was then categorized into quartiles. Individual comorbidities were analyzed separately and combined under a binary yes/no variable called “any documented disease” that included the following medical histories: cancer, diabetes, heart disease, hyperlipidemia, hypertension, renal disease, respiratory disease, and stroke. Arrest etiology was either cardiac or non-cardiac. First monitored rhythm was shockable (ventricular tachycardia, ventricular fibrillation, unknown shockable rhythm) or non-shockable (pulseless electrical activity, asystole, unknown non-shockable rhythm). For neurological recovery, Cerebral Performance Category (CPC) score was dichotomized into favorable (CPC 1–2) or unfavorable (CPC 3–5) outcomes.

Classification of hospitals

Hospital arrest volume was treated as a surrogate measure for hospital experience in post-arrest care. After determining the quartile cut-offs for the distribution of arrest volume among our hospital population, hospitals were assigned to quartiles. Hospitals with higher OHCA admissions were hypothesized to deliver greater care translating to better outcomes. Arrest volume quartiles were determined by patient data aggregation at the hospital level and calculation of the number of post-arrest episodes within each hospital. After examining the receiving volume distribution of hospitals and determining quartile cutoffs, a variable representing the quartile category was assigned to each of the 48 hospitals. One hospital with a volume of 49 cases was manually moved to quartile 1 [40–49 cases] after initial automatic assignment to quartile 2, explaining the presence of 13 hospitals in that group. This change did not contribute to any differences in results.

Statistical analysis

Descriptive statistics were used to summarize patient characteristics, arrest circumstances, and hospital interventions. When the normality assumption was violated (Shapiro-Wilk normality test), continuous variables were reported as medians (interquartile range) instead of means \pm standard deviation. Categorical variables were presented as frequencies (percentages).

For hospital-level analyses, data that were originally categorical at the patient-level were aggregated into counts and percentages.

Percent delivery of interventions, survival, and favorable neurological outcome were calculated and represented by error bar plots.

Population differences between hospitals with low or high survival, or across volume quartiles were examined at the patient level using chi-square tests (categorical data), and the Mann-Whitney U or Kruskal-Wallis H nonparametric tests (continuous data). All statistical tests were 2-sided, and a P-value of <0.05 was statistically significant. Multiple logistic regression models were created to adjust for demographic and clinical characteristics that were suspected to be associated or had a univariate correlation ($P < 0.1$) with our study outcomes. Age, gender, and race were included in the model regardless of statistical significance. Excluded variables from the model did not meet the above criteria. After adjusting for patient and arrest characteristics, we assessed the effects of volume quartiles and post-arrest interventions on survival outcomes. Discrimination and goodness-of-fit of models were evaluated using the area under the receiver operating characteristic (ROC) curve and the Hosmer-Lemeshow test respectively. Data were managed and analyzed using standard statistical software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23, Armonk, NY:IBM Corp).

Results

Study population

Our original dataset was comprised of 19,649 cases from 149 hospitals within PA. After exclusion of cases not meeting inclusion criteria, 3512 cases admitted to 48 hospitals were included in our analysis (Fig.1).

Initial analysis showed a wide variation in unadjusted rates of survival [24%–65%, mean 40.86 ± 10.27] and favourable neurological outcome [15%–56%, mean 33.68 ± 10.9] across hospitals (Fig.2).

As shown in Table 1, the post-arrest patient population had a median age of 63 (IQR 22) years, 60.3% were male, 71.1% were witnessed arrests, 38.7% received layperson CPR, and 32.6% had an initial shockable rhythm. TTM and coronary angiography were performed in 42.3% and 29.2% of cases respectively. Overall survival and neurological recovery were 41.3% and 34.2%, respectively.

Comparison of low vs high performers

Hospitals with higher survival rates (\geq mean hospital survival rate of 40.8%) treated a significantly higher percentage of patients who were white with favorable prehospital arrest characteristics (witnessed arrests, lay person CPR administration, and shockable rhythms). This population also had a significantly lower rate of EMS-placed advanced airways and drug administration, but a higher rate of intravenous catheter placement and mechanical CPR use. A significantly higher percentage of patients received post-arrest care in this group, with the exception of TTM. (Table 1).

Comparison of key indicators between hospitals quartiles (Q1-Q4)

The 48 hospitals were then divided into quartiles depending on their receiving OHCA volumes (Table 2). Receiving volume was normally distributed within each quartile. The lowest volume quartile (Q1) received 16.4% of total cases with a low frequency of arrests (40–49

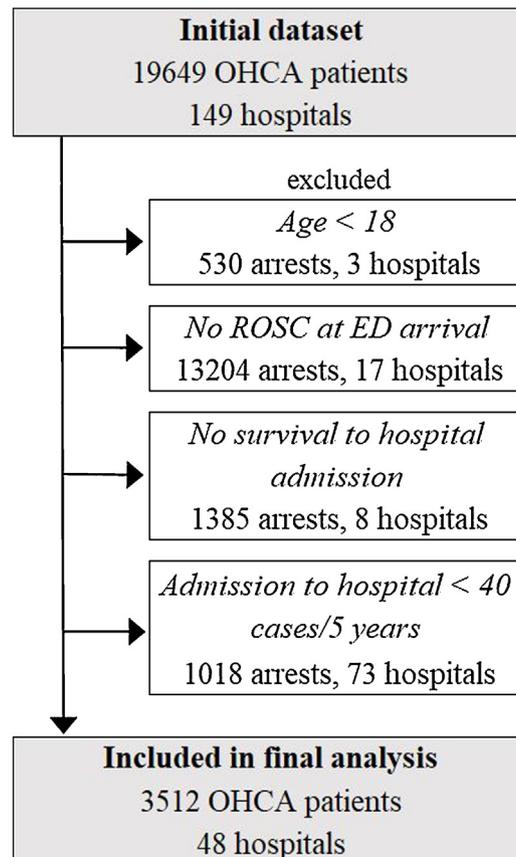


Fig. 1 – Flowchart of inclusion criteria for data analysis.

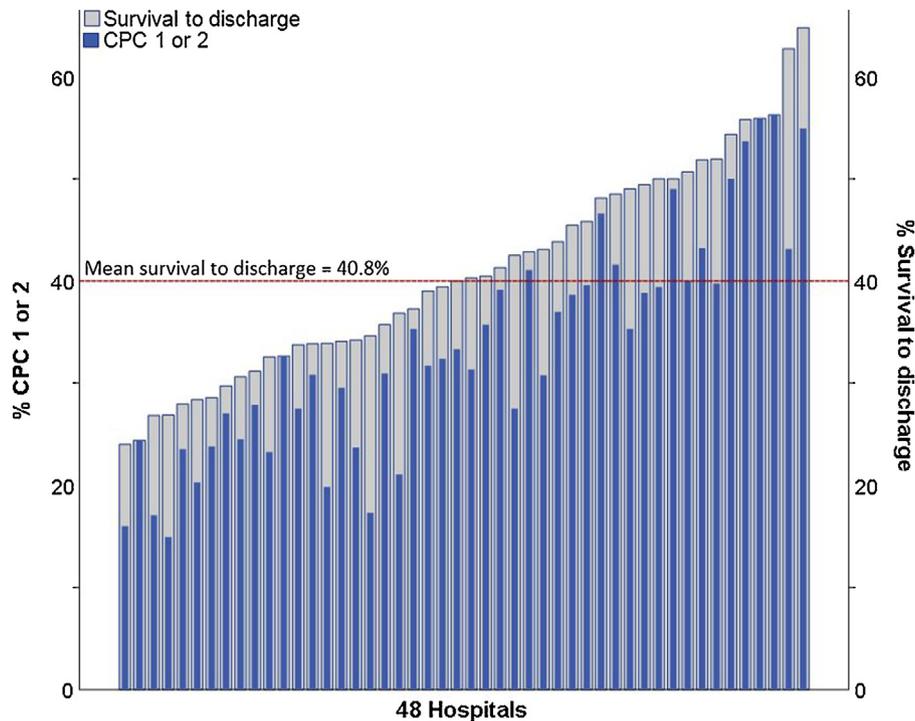


Fig. 2 – Percentage of patients with survival to discharge and favourable CPC scores (1 or 2) across 48 included hospitals.

Table 1 – Hospital and patient demographic, pre-hospital, and post-arrest characteristics and outcomes across low vs. high survival hospital groups.

Continuous var., Mdn (IQR)	All hospitals N = 48	Hospitals with survival < 40% N = 23	Hospitals with survival ≥ 40% N = 25	p-value
Age	63 (22)	63 (23)	63 (22)	0.416
Volume	65.5 (34)	74 (82)	81 (40)	0.402
Categorical var., N (%)				
Male	2117 (60.3)	974 (58.5)	1143 (61.9)	0.04
Race: white	2002 (57.0)	818 (49.1)	1184 (64.1)	<0.001
Any documented disease	1952 (55.6)	875 (52.6)	1077 (58.3)	0.001
Witnessed arrest	2496 (71.1)	1147 (68.9)	1349 (73.0)	0.007
CPR: Lay person	1359 (38.7)	539 (32.4)	820 (44.4)	<0.001
Arrest etiology: cardiac	2684 (76.4)	1263 (75.9)	1421 (76.9)	0.45
First rhythm: shockable	1145 (32.6)	467 (28.0)	678 (36.7)	<0.001
Advanced airway placed	2492 (71.0)	1269 (76.3)	1223 (66.3)	<0.001
IV access	2278 (64.9)	990 (59.5)	1288 (69.7)	<0.001
Drugs administered	2697 (76.8)	1382 (83.0)	1315 (71.2)	<0.001
Mechanical CPR device used	773 (22.0)	305 (18.3)	468 (25.4)	<0.001
Arrest to ED time quartiles				
0:00–31:00 min	905 (26.1)	456 (27.5)	449 (24.8)	
31:01–38:00 min	864 (24.9)	407 (24.5)	457 (25.2)	
38:17–47:34 min	835 (24.0)	412 (24.8)	423 (23.3)	
47:44–142:00 min	870 (25.0)	386 (23.2)	484 (26.7)	
TTM initiated	1465 (42.3)	769 (46.9)	696 (38.2)	<0.001
Coronary angiography	948 (29.2)	403 (26.3)	545 (31.7)	0.001
Coronary stenting	500 (15.4)	198 (13.0)	302 (17.5)	<0.001
ICD placement	327 (10.1)	113 (7.4)	214 (12.5)	<0.001
CABG	70 (2.1)	28 (1.8)	42 (2.4)	0.25
Transfers to other hospitals	332 (9.5)	206 (12.4)	126 (6.8)	<0.001
Survival to discharge	1451 (41.3)	545 (32.7)	906 (49.1)	<0.001
CPC 1 or 2	1200 (34.2)	424 (25.5)	776 (42.0)	<0.001

Var., variable; Mdn, median; IQR, interquartile range; N, frequency; CPR, cardiopulmonary resuscitation; IV, intravenous; ED, emergency department; TTM, Targeted temperature management; ICD, implantable cardioverter defibrillator; CABG, Coronary artery bypass grafting; CPC, cerebral performance category.

Table 2 – Hospital and patient demographic, pre-hospital, and post-arrest characteristics and outcomes across the volume quartile categories.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p-value
Range of arrests/5 yrs.	40–49	50–65	66–81	84–205	
Hospitals, N	13	11	12	12	
Arrest volume/5 yrs., Mean ± SD	44.38 ± 3.25	55.73 ± 5.08	72.42 ± 5.01	121.08 ± 36.08	<0.000
Patients, N (%)	577 (16.4)	613 (17.5)	869 (24.7)	1453 (41.4)	
Age, Mdn (IQR)	64 (22)	65 (23)	63 (22)	63(23)	0.442
Categorical var., N (%)					
Male	371 (64.3)	354 (57.7)	525 (60.4)	867 (59.7)	0.12
Race: white	386 (66.9)	369 (60.2)	477 (54.9)	770 (53.0)	<0.001
Any documented disease	342 (59.3)	314 (51.2)	474 (54.5)	822 (56.6)	0.03
Witnessed arrest	421 (73.0)	425 (69.3)	624 (71.8)	1026 (70.6)	0.51
CPR: Lay person	232 (40.2)	244 (39.8)	316 (36.4)	567 (39.0)	0.40
Arrest etiology: cardiac	437 (75.7)	460 (75.0)	663 (76.3)	1124 (77.4)	0.67
First rhythm: shockable	194 (33.6)	186 (30.3)	281 (32.3)	484 (33.3)	0.56
Advanced airway placed	422 (73.4)	408 (66.7)	651 (74.9)	1011 (69.6)	0.002
IV access	345 (59.8)	411 (67.0)	559 (64.3)	963 (66.3)	0.02
Drugs administered	450 (78.0)	440 (71.8)	703 (80.9)	1104 (76.0)	<0.001
Mechanical CPR device used	161 (27.9)	85 (13.9)	137 (15.8)	390 (26.9)	<0.001
Arrest to ED time quartiles					<0.001
0:00–31:00 min	164 (29.5)	200 (32.8)	198 (23.0)	343 (23.7)	
31:01–38:00 min	146 (26.3)	156 (25.6)	202 (23.4)	360 (24.9)	
38:17–47:34 min	123 (22.2)	143 (23.5)	206 (23.9)	363 (25.1)	
47:44–142:00 min	122 (22.0)	110 (18.1)	256 (29.7)	382 (26.4)	
TTM initiated	215 (38.5)	253 (41.7)	376 (43.9)	621 (43.2)	0.19
Coronary angiography	155 (31.0)	153 (26.7)	241 (31.2)	399 (28.4)	0.22
Coronary stenting	77 (15.4)	78 (13.5)	137 (17.6)	208 (14.9)	0.20
ICD placement	59 (12.0)	54 (9.5)	70 (9.1)	144 (10.3)	0.38
CABG	7 (1.4)	11 (1.9)	15 (1.9)	37 (2.6)	0.34
Transfers to other hospitals	152 (26.3)	62 (10.1)	48 (5.5)	70 (4.8)	<0.001
Survival to discharge	219 (38.0)	255 (41.6)	358 (41.2)	619 (42.6)	0.29
CPC 1 or 2	188 (32.6)	200 (32.6)	287 (33.0)	525 (36.1)	0.23

Var., variable; *Mdn*, median; *IQR*, interquartile range; *N*, frequency; *CPR*, cardiopulmonary resuscitation; *IV*, intravenous; *ED*, emergency department; *TTM*, Targeted temperature management; *ICD*: implantable cardioverter defibrillator; *CABG*: Coronary artery bypass grafting; *CPC*, cerebral performance category.

cases). Hospitals in the highest volume quartile (Q4) received 41.4% of total cases with the highest arrest frequency (84–205 cases.) With increasing quartiles, hospitals captured a greater percentage of total arrests.

Across the four hospital categories, age and gender were not significantly different (Table 2). In comparison to lower quartiles, higher quartiles had significantly less white patients, and longer arrest to ED times (26.4% in Q4 vs 18.1% in Q2 for 47–142 min group). Despite the significant differences shown in other care process variables such as advanced airway placement, drug administration, mechanical CPR use, and transfer rates, no discernible trends in the data were appreciated. (Table 2).

Fig. 3 summarizes the frequency of provision of post-arrest care interventions by percentage of treated patients across the quartiles. Chi-square testing at the population level did not show any significant differences in post-arrest care provision between groups, although varied degrees of dispersion are seen on error bar representation of the data (Fig. 3). Higher volumes hospitals had potentially less variation in delivery of care as shown by the standard deviation bars. Percent TTM provision for hospitals in Q1 [10.4%–83.673%, SD = 25.5] was more varied than for hospitals in Q4 [22.8%–60.9%, SD = 12.4]. Similar results were observed for coronary angiography, coronary stenting, and ICD placement, where Q4 hospital performance was generally closer to the quartile mean value.

Survival and good neurological recovery rates (Fig. 3) showed a positive trend towards higher quartiles, although non-significant ($p=0.295$ for survival, $p=0.232$ for CPC 1 or 2). Levene's test of variances did not show a significant difference in the degree of dispersion of survival outcomes or post-arrest interventions except for ICD placement.

Association of arrest volume with survival and neurological outcome

Table 3 shows the ORs and 95% CIs for survival to discharge and favorable CPC score. Compared to Q1, odds of patient survival at Q3 or Q4 hospitals were 42% and 33% higher respectively (Q3: OR, 1.42; 95% CI, 1.08–1.87; Q4: OR, 1.33; 95% CI, 1.03–1.71) after adjusting for demographics (age, gender, race, medical history), arrest characteristics (witnessed arrest, rhythm type), and pre-hospital care (advanced airway placement, IV access, drug administration, and time to ED quartiles). Similarly, odds of a good neurological outcome at discharge was 32% higher in Q4 (OR, 1.32; 95% CI, 1.01–1.71).

Additional adjustment for post-arrest interventions (TTM, coronary angiography, coronary stenting) further highlighted this volume-outcome association with 43% (OR, 1.43; 95% CI, 1.08–1.89) and 51% (OR, 1.51; 95% CI, 1.11–2.04) higher odds of survival and good

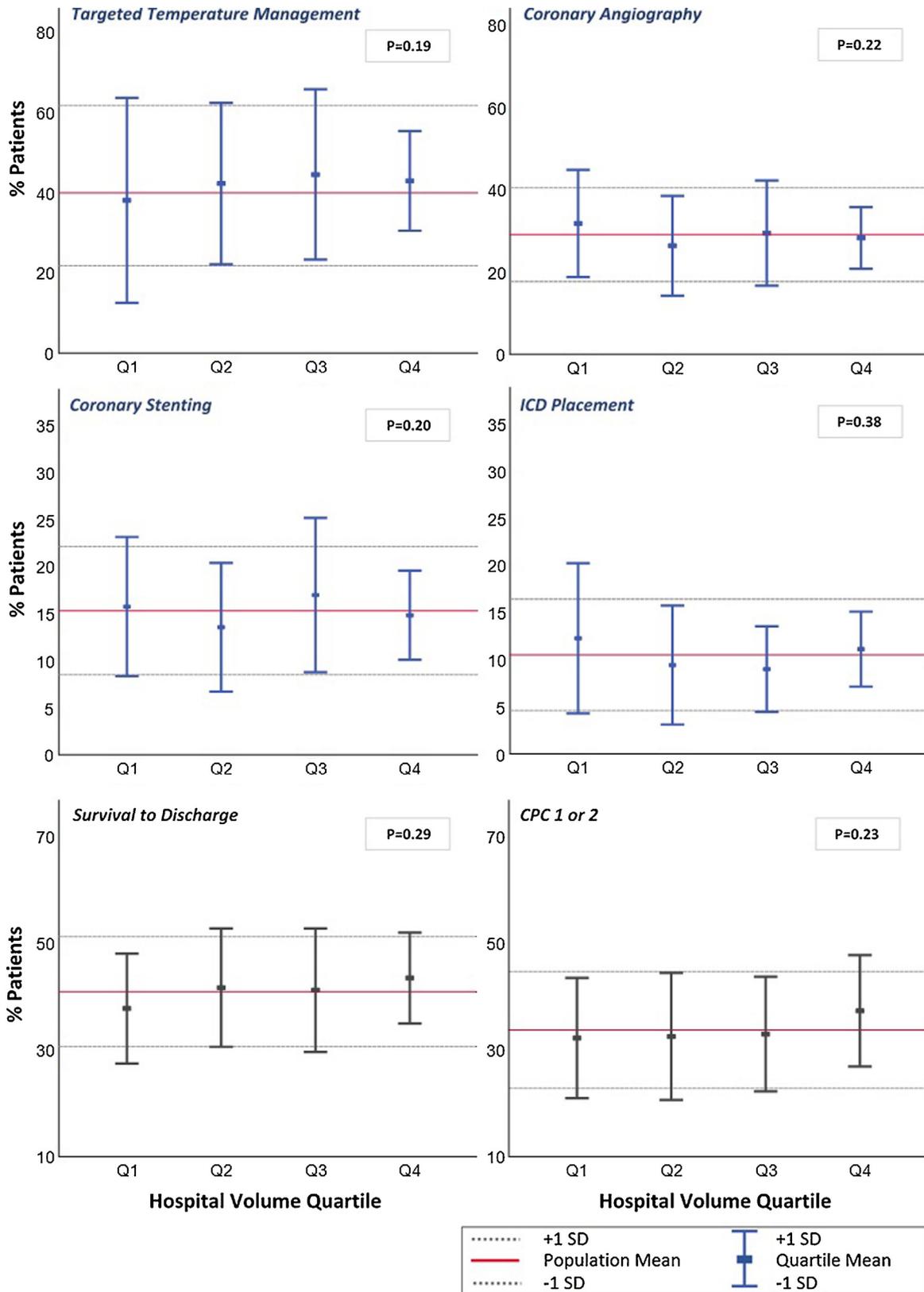


Fig. 3 – Percent post-arrest care provision, survival to discharge, and favorable neurological outcome (CPC 1 or 2) across hospital quartiles.

Table 3 – Multivariate logistic regression model for survival to discharge and CPC score of 1 or 2 for patients admitted to hospitals with a minimum of 40 arrests/5 years (48 hospitals).

Survival to discharge, logistic regression models, OR (95% CI)

	Crude	p-value	Adjusted for quartiles ^a	p-value	Adjusted for quartiles and post-arrest care ^a	p-value
Volume quartile		0.29		0.03		0.06
Q1	1.00		1.00		1.00	
Q2	1.16 (0.92, 1.46)	0.20	1.08 (0.79, 1.46)	0.62	1.18 (0.84, 1.63)	0.33
Q3	1.15 (0.92, 1.42)	0.22	1.42 (1.08, 1.87)	0.01	1.39 (1.03, 1.90)	0.03
Q4	1.21 (0.99, 1.47)	0.055	1.33 (1.03, 1.71)	0.03	1.43 (1.08, 1.89)	0.01
TTM	0.54 (0.47, 0.62)	<0.001	–		0.56 (0.46, 0.68)	<0.001
Cor. Angiography	5.39 (4.57, 6.36)	<0.001	–		3.54 (2.70, 4.65)	<0.001
Cor. Stenting	4.52 (3.66, 5.58)	<0.001	–		0.99 (0.71, 1.37)	0.93

CPC 1 or 2, Logistic regression models, OR (95% CI)

	Crude	p-value	Adjusted for quartiles ^a	p-value	Adjusted for quartiles and Post-arrest care ^a	p-value
Volume quartile		0.23		0.05		0.003
Q1	1.00		1.00		1.00	
Q2	1.00 (0.78, 1.27)	0.99	0.83 (0.59, 1.16)	0.28	0.93 (0.64, 1.33)	0.67
Q3	1.02 (0.81, 1.27)	0.86	1.22 (0.91, 1.65)	0.19	1.19 (0.86, 1.68)	0.29
Q4	1.17 (0.95, 1.43)	0.13	1.32 (1.01, 1.74)	0.04	1.51 (1.11, 2.04)	0.009
TTM	0.48 (0.41, 0.56)	<0.001	–		0.43 (0.34, 0.54)	<0.001
Cor. Angiography	6.58 (5.57, 7.77)	<0.001	–		4.98 (3.73, 6.65)	<0.001
Cor. Stenting	5.27 (4.29, 6.46)	<0.001	–		1.06 (0.76, 1.48)	0.728

CI, confidence interval; OR, odds ratio; Q, quartiles; TTM, targeted temperature management, Cor., Coronary; ICD, implantable cardioverter defibrillator.

^a Adjusted for age, gender, race, diabetes, witnessed arrest, rhythm type, advanced airway placement, IV access, drug administration, and time to ED quartiles.

neurological outcome respectively in the highest compared to the lowest quartiles.

Witnessed arrests, initial shockable rhythms, and prehospital IV access were associated with higher odds for a favorable outcome. Diabetes, prehospital advanced airway placement, drug administration, and greater arrest-to-ED times decreased the odds. TTM had a significant inverse relation with favorable prognosis (Survival: OR 0.56; 95% CI, 0.46–0.68; CPC: OR 0.43; 95% CI, 0.34–0.54 respectively). After simultaneous adjustment for coronary angiography (Survival: OR 3.54; 95% CI, 2.7–4.6; CPC score: OR 4.98; 95% CI, 3.7–6.6), the positive association between stenting and outcomes did not reach statistical significance. ICD placement was not included in our final model since only patients who survived likely received the treatment. Sensitivity analysis for minimum hospital population supported the findings of favorable neurological outcome associated with higher quartile hospitals, but not for survival to discharge (See Supplementary Table 4). The predictive performance of the final model (adjusted for quartiles and post-arrest care) was good with an area under the ROC curve of 0.79 for survival to discharge, and 0.82 for neurological recovery. The Hosmer–Lemeshow statistic showed a good agreement between predicted and observed rates ($p = 0.18$ for survival, $p = 0.10$ for neurological recovery).

Discussion

Significant variation exists in post-cardiac arrest care and survival outcomes in PA. The odds of survival and neurological recovery were up to 43% and 51% increased in higher quartile hospitals respectively, independent of the confounding effects of demographic and prehospital factors. There also appears to be greater uniformity in

post-arrest care at higher volume centers. This analysis is consistent with previous research highlighting the challenges in isolating the confounding influences in post-arrest care analysis and volume-outcome associations,^{17,23–25} however our results support regionalization of OHCA care to high volume centers for improved patient survival and neurological recovery.

Since volume of patients treated serves as a reliable index for hospital expertise and case familiarity across different disease states, a positive volume-outcome relationship was the premise for stratification of hospitals into volume quartiles.^{8,11,26–28} Our classification method was further supported by study results showing improved adherence to OHCA guideline-driven protocols or survival in higher volume ICUs.^{8,11} Demographic, pre-hospital, and post-arrest factors did not trend favourably in a consistent pattern from lower to higher quartiles (Table 2) since volume alone cannot explain various performance metrics influenced by complex confounders.

The results of our study are consistent with previous work. A study by Worthington et al. found significant variability in successful TTM ranging between 0% and 61%.¹¹ Overall mortality varied by type of hospital in one national US study, with odds ranging from 0.58 (large rural teaching hospital) to 0.78 (small rural non-teaching hospital).²⁹ Another CARES registry study reported survival rates ranging between 3.4% to 22% among 132 US counties.⁷

This variation may partially be explained by inherent patient and prehospital level differences, as seen in our data comparing hospitals with high or low performance. For example, hospitals with better survival outcomes had a higher percentage of white patients and lay person CPR rates. As previous research has highlighted,³⁰ demographic and socioeconomic disparities contributing to poor CPR training may provide one explanation of varied outcomes. EMS case selection bias is another confounder; patients with favourable

prognoses were conceivably transported to better performing hospitals as shown by the higher percentage of patients with shockable rhythms in hospitals with high vs. low survival (36.7% vs 28%, $p < 0.001$). At the hospital level, selection and survival biases interfere with patient selection for and timely provision of post-arrest care. Patients with better prognosis likely received coronary angiography, stenting, ICD placement, and CABG procedures at higher rates. TTM may have been reserved for patients with delayed recovery times, explaining the $OR < 1$ in our results. Higher transfer rates, 12.4% and 26.3%, in lower performing and small volume hospitals respectively, introduces selection bias to higher volume centres receiving more patients, despite no correlation seen with outcomes in our results. Adjustment for such influences however isolated a discrete volume-outcome relationship.

Identifying factors associated with better outcomes is necessary. However, if this is difficult to achieve across hospitals or regions due to resource limitations, then transport to cardiac centres may be a reasonable alternative. In Arizona, a statewide implementation of a regionalized system of care was significantly associated with improved TTM delivery [0–44%] and catheterization [11.7–30.7%] with an overall increase in survival from 8.9% to 14.4% ($OR = 2.22$; [95% CI 1.47–3.34]).¹⁷ Despite possible longer transport durations, a higher adherence to standards of care and improved survival outcomes in specialized centres remains a practical solution.^{31,32}

Our analysis has several limitations primarily related to unavailable data such as hospital location (urban or rural), academic status, availability of catheterization centres, number of hospital beds, and provider level volume. More challenging factors to control for such as organizational cultures or the presence of domain experts may also play into favourable results. Opinion leaders in institutions may be the sole drivers in some instances, reinforcing a collaborative culture for quality of care against barriers to implementation of post-arrest care.^{33,34} TTM is yet another domain underlying the variability due to varied standards for patient selection, time to initiation, target temperature, and duration of treatment.³⁵ Conversely, we consider the confinement of our study to patients arriving with ROSC and survival to admission to moderate to high volume centers as a study strength that helped reduce the influence of prehospital care factors and potentially outlying data of low-volume hospitals on our analysis.

Conclusions

Our aim was to explore avenues for improvement and identify elements conferring a better performance profile to hospitals. Consistent with other many disease states, cardiac arrest survival and good neurological recovery rates were positively associated with hospital receiving volume, and a propensity for greater consistency of care was observed in higher volume facilities. This may be explained by greater procedural familiarity and availability of resources at high volume facilities. Our results support regionalizing care to tertiary centers with more uniform guideline-driven protocols and higher rates of post-arrest interventions.

Conflicts of interest

Steve Balian, David Buckler, and Abhishek Bhardwaj report no conflicts of interest related to the subject matter discussed in this

manuscript. Audrey Blewer has received funding from the American Heart Association. Benjamin Abella reports the following conflicts: Research funding from the American Heart Association, National Institutes of Health, Patient Centered Outcomes Research Institute and CR Bard; speaking honoraria from CR Bard and Stryker.

Acknowledgements

The authors thank member site EMS agencies and hospitals for their contributions to CARES (<https://mycares.net/sitepages/map.jsp>) and this project. Steve Balian would also like to acknowledge the training received under the Scholars in Health Research Program (SHARP) in clinical and translational research.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.resuscitation.2019.02.004>.

REFERENCES

1. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation* 2018;137:e67–e492.
2. Callaway CW, Donnino MW, Fink EL, et al. Part 8: post-cardiac arrest care: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132:S465–482.
3. Dumas F, White L, Stubbs BA, Cariou A, Rea TD. Long-term prognosis following resuscitation from out of hospital cardiac arrest: role of percutaneous coronary intervention and therapeutic hypothermia. *J Am Coll Cardiol* 2012;60:21–7.
4. Garcia S, Drexel T, Bekwelem W, et al. Early access to the cardiac catheterization laboratory for patients resuscitated from cardiac arrest due to a shockable rhythm: the Minnesota resuscitation consortium twin cities unified protocol. *J Am Heart Assoc* 2016; doi:<http://dx.doi.org/10.1161/JAHA.115.002670>.
5. Neumar RW, Nolan JP, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A consensus statement from the International Liaison Committee on Resuscitation (American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; and the Stroke Council. *Circulation* 2008;118:2452–83.
6. Nichol G, Aufderheide TP, Eigel B, et al. Regional systems of care for out-of-hospital cardiac arrest: a policy statement from the American Heart Association. *Circulation* 2010;121:709–29.
7. Girotra S, van Diepen S, Nallamothu BK, et al. Regional variation in out-of-hospital cardiac arrest survival in the United States. *Circulation* 2016;133:2159–68.
8. Carr BG, Kahn JM, Merchant RM, Kramer AA, Neumar RW. Inter-hospital variability in post-cardiac arrest mortality. *Resuscitation* 2009;80:30–4.
9. Albaeni A, Beydoun MA, Beydoun HA, et al. Regional variation in outcomes of hospitalized patients having out-of-hospital cardiac arrest. *Am J Cardiol* 2017;120:421–7.

10. Nichol G, Thomas E, Callaway CW, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA* 2008;300:1423–31.
11. Worthington H, Pickett W, Morrison LJ, et al. The impact of hospital experience with out-of-hospital cardiac arrest patients on post cardiac arrest care. *Resuscitation* 2017;110:169–75.
12. Bobrow BJ, Kern KB. Regionalization of postcardiac arrest care. *Curr Opin Crit Care* 2009;15:221–7.
13. Nichol G, Soar J. Regional cardiac resuscitation systems of care. *Curr Opin Crit Care* 2010;16:223–30.
14. Kronick SL, Kurz MC, Lin S, et al. Part 4: systems of care and continuous quality improvement: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132:S397–413.
15. Mooney MR, Unger BT, Boland LL, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest: evaluation of a regional system to increase access to cooling. *Circulation* 2011;124:206–14.
16. Soholm H, Wachtell K, Nielsen SL, et al. Tertiary centres have improved survival compared to other hospitals in the Copenhagen area after out-of-hospital cardiac arrest. *Resuscitation* 2013;84:162–7.
17. Spaite DW, Bobrow BJ, Stolz U, et al. Statewide regionalization of postarrest care for out-of-hospital cardiac arrest: association with survival and neurologic outcome. *Ann Emerg Med* 2014;64: 496–506.e1.
18. McNally B, Stokes A, Crouch A, Kellermann AL, CARES Surveillance Group. CARES: Cardiac Arrest Registry to Enhance Survival. *Ann Emerg Med* 2009;54: 674–683.e2.
19. Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. *Circulation* 2015;132:1286–300.
20. Mader TJ, Nathanson BH, Millay S, et al. Out-of-hospital cardiac arrest outcomes stratified by rhythm analysis. *Resuscitation* 2012;83:1358–62.
21. Naim MY, Burke RV, McNally BF, et al. Association of bystander cardiopulmonary resuscitation with overall and neurologically favorable survival after pediatric out-of-hospital cardiac arrest in the United States: a report from the cardiac arrest registry to enhance survival surveillance registry. *JAMA Pediatr* 2017;171:133–41.
22. Edgren E, Hedstrand U, Kelsey S, Sutton-Tyrrell K, Safar P. Assessment of neurological prognosis in comatose survivors of cardiac arrest. BRCT I Study Group. *Lancet* 1994;343:1055–9.
23. Johnson NJ, Salhi RA, Abella BS, Neumar RW, Gaieski DF, Carr BG. Emergency department factors associated with survival after sudden cardiac arrest. *Resuscitation* 2013;84:292–7.
24. Stub D, Smith K, Bray JE, Bernard S, Duffy SJ, Kaye DM. Hospital characteristics are associated with patient outcomes following out-of-hospital cardiac arrest. *Heart* 2011;97:1489–94.
25. Cudnik MT, Sasson C, Rea TD, et al. Increasing hospital volume is not associated with improved survival in out of hospital cardiac arrest of cardiac etiology. *Resuscitation* 2012;83:862–8.
26. Amato L, Colais P, Davoli M, et al. Volume and health outcomes: evidence from systematic reviews and from evaluation of Italian hospital data. *Epidemiol Prev* 2013;37:1–100.
27. Norderhaug I, Krogstad U, Ingebrigtsen T, Søreide O, Wiseth R, Olav Myhre H. The Influence of Hospital or Physician Volume on Quality of Health Care. Report from Kunnskapscenteret no. 10–2007. Oslo, Norway: Knowledge Centre for the Health Services at The Norwegian Institute of Public Health (NIPH); 2007. <http://www.ncbi.nlm.nih.gov/books/NBK464808/>.
28. Nimptsch U, Mansky T. Hospital volume and mortality for 25 types of inpatient treatment in German hospitals: observational study using complete national data from 2009 to 2014. *BMJ Open* 2017; e016184-2017-016184.
29. Carr BG, Goyal M, Band RA, et al. A national analysis of the relationship between hospital factors and post-cardiac arrest mortality. *Intensive Care Med* 2009;35:505–11.
30. Blewer AL, Ibrahim SA, Leary M, et al. Cardiopulmonary resuscitation training disparities in the United States. *J Am Heart Assoc* 2017; doi: <http://dx.doi.org/10.1161/JAHA.117.006124>.
31. Cudnik MT, Schmicker RH, Vaillancourt C, et al. A geospatial assessment of transport distance and survival to discharge in out of hospital cardiac arrest patients: implications for resuscitation centers. *Resuscitation* 2010;81:518–23.
32. Spaite DW, Stiell IG, Bobrow BJ, et al. Effect of transport interval on out-of-hospital cardiac arrest survival in the OPALS study: implications for triaging patients to specialized cardiac arrest centers. *Ann Emerg Med* 2009;54:248–55.
33. Williams D, Calder S, Cocchi MN, Donnino MW. From door to recovery: a collaborative approach to the development of a post-cardiac arrest center. *Crit Care Nurse* 2013;33:42–54.
34. Wang HE, Thomas JJ, James D, et al. Post-cardiac arrest therapeutic hypothermia: overcoming the barrier of workplace culture and other implementation lessons. *Jt Comm J Qual Patient Saf* 2011;37:425–32.
35. Camp-Rogers TR, Sawyer KN, McNicol DR, Kurz MC. An observational study of patient selection criteria for post-cardiac arrest therapeutic hypothermia. *Resuscitation* 2013;84:1536–9.